Selective *meso*-monobromination of 5,15-diarylporphyrins via organopalladium porphyrins

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ABSTRACT: The selective *meso*-monobromination of 5,15-diarylporphyrins is difficult to achieve and extensive chromatography is required to obtain pure products. A sequence of (i) dibromination, (ii) selective monoinsertion of [Pd(dppe)] [dppe = 1,2-bis(diphenylphosphino)ethane] and (iii) hydrodepalladation using methanolic base affords pure monobromoporphyrins in typically ≥60% overall yield without isolation of the organopalladium porphyrin. Monobromo derivatives of even highly lipophilic 5,15-diarylporphyrins are thus readily available without tedious, expensive and environmentally undesirable chromatography.

KEYWORDS: porphyrins, organometallic, palladium, bromination.

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INTRODUCTION

The bromination of 5,15-diarylporphyrins has assumed singular importance in recent years as many workers have exploited reactions at the *meso* positions of these versatile substrates. For example, palladium-catalyzed couplings of bromoporphyrins have been used for attaching a variety of groups to the *meso* carbon(s) using Pd-catalyzed C–C and C–X couplings [1] This work has resulted in a resurgence of interest in porphyrin functionalization and multiporphyrin construction, leading to a bewildering array of novel and interesting structures. This chemistry depends on the intermediacy of *meso*-η^1-palladio(II) porphyrins, compounds that we first isolated and reported in 1998 [2]. Since then, we have investigated the formation, structures and utility of these novel organopalladium porphyrins and their more robust platinum(II) analogues [3-6] The organometallic moiety has usually been supported by tertiary phosphine ligands, either monodentate or bidentate. Recently we reported the first examples with chelating diamines [6] and the use of this fragment for the generation of multi-porphyrin coordination arrays [7]

The NBS bromination [1a] of the unsubstituted 5,15-diphenylporphyrin free base H_2DPP, while very rapid, is not selective, and use of one equivalent of NBS results in a mixture of the desired 5-bromoporphyrin, the 5,15-dibromoporphyrin and unreacted H_2DPP. On the other hand, *di*bromination of most diarylporphyrin substrates can be readily achieved in near quantitative yields using 2.1 equivalents of NBS.

For convenient study of oligoporphyrins, substrates with solubilizing substituents are required, particularly 5,15-bis(3',5'-di-*tert*-butylphenyl)porphyrin or 5,15-bis(3',5'-dialkoxyphenyl)porphyrins. With these substrates, obtaining high yields of the monobromo derivatives is problematic, as more stringent chromatography involving large amounts of silica gel, solvents and time is necessary. Several authors have reported improvements to the bromination procedure, and isolated yields of up to 60% of monobromoporphyrin have been reported [1c,1e,1l]. For more complex coupling regimes using these soluble building blocks, it is often very inconvenient if dibromo compound is present in the coupling mixture. One way to circumvent this problem, if applicable, is to use 5,10,15-triaryl- or 5-alkyl-10,20-diarylporphyrins that have only one *meso* carbon available for bromination. Such porphyrins can be made either by classical mixed aldehyde syntheses or by the methods of Senge using arylation(alkylation) by organolithiums followed by protonation and rearomatization [8]. We were seeking ways to alleviate the burden of chromatography when lipophilic monobromo substrates are required for syntheses involving a free *meso* carbon, and now report the stoichiometric use of organopalladium complexes as intermediates in overall selective monobromination of a suite of 5,15-diarylporphyrins.

EXPERIMENTAL

General

Syntheses involving zerovalent metal precursors were carried out in an atmosphere of high-purity argon using conventional Schlenk techniques. Dibromoporphyrins were prepared by the literature method for diphenylporphyrin [1a] using 2.1 equivalents of NBS in chloroform in the presence of pyridine. Compounds **2b** and **2d** are previously unreported, and their characterisation data are given below. All other reagents and ligands were used as received from Sigma-Aldrich. Toluene was AR grade, stored over sodium wire, and degassed by heating and purging with argon at 100 °C. All other solvents were AR grade, and dichloromethane and chloroform were stored over anhydrous sodium carbonate. Analytical TLC was performed using Merck silica gel 60 F254 plates and column chromatography was performed using Merck silica gel (230-400 mesh). NMR spectra were recorded on Bruker Avance 400 MHz or Varian Unity 300 MHz instruments in $CDCl_3$ solutions, using $CHCl_3$ as the internal reference at 7.26 ppm for ^{1}H spectra, and external 85% H_3PO_4 as the reference for proton-decoupled ^{31}P spectra. UV-visible spectra were recorded on a Cary 3

spectrometer in dichloromethane solutions. For mass spectra, the most abundant ion in the cluster (to the stated precision) is quoted. Mass spectra were recorded on (i) Shimadzu Kompact in dithranol matrix (MALDI-TOF), (ii) Jeol JMS-600H in m-nitrobenzyl alcohol (FAB) (The Institute of Scientific and Industrial Research, Osaka University) and (iii) Bruker BioApex 47e FTMS with an Analytica Electrospray Source (HR-ESI) (Monash University). In the last method, the samples were dissolved in dichloromethane and diluted with either dichloromethane/methanol 1:1 or methanol and solutions were introduced into the source by direct infusion (syringe pump) at 60 μL/h, with a capillary voltage of 80 V. The instrument was calibrated using internal NaI.

Synthesis

5,15-Dibromo-10,20-bis(3',5'-dimethylphenyl)porphyrin 2b. Porphyrin **1b** (60.0 mg, 0.116 mmol) was dissolved in $CHCl_3$ (120 mL) and pyridine (480 μL). After cooling to 0°, NBS (43.0 mg, 0.242 mmol, 2.1 eq) was added. After 30 min, the reaction reached completion and was quenched with acetone (10 mL). The solvent was evaporated, and the product was washed with several portions of methanol. The compound was recrystallized from toluene/MeOH to give **2b** as purple crystals (78 mg, 0.115 mmol, 99%). ^{1}H NMR: δ 9.61, 8.88 (both d, 4H, *J* 4.8 Hz, β), 7.78 (br s, 4H, Ar), 7.43 (br s, 2H, Ar), 2.62 (s, 12H, CH_3), –2.73 (br s, 2H, NH); UV/vis: λ_{max}(ε/10^3 $M^{-1}cm^{-1}$) 421 (353), 487 (4.3), 521 (16.8), 556 (11.3), 600 (5.1), 658 (5.8) nm; MALDI-TOF MS: 677.1 (M+H requires 677.1); Anal. Calcd. C, 63.92; H, 4.17; N, 8.28; Found C, 64.16; H, 4.35; N, 8.54%.

5,15-Dibromo-10,20-bis[3',5'-bis(isoamyloxy)phenyl]porphyrin 2d. Porphyrin **1d** (82.0 mg, 0.102 mmol) was dissolved in $CHCl_3$ (30 mL) and pyridine (120 μL). After cooling to 0°, NBS (38.0 mg, 0.214 mmol, 2.1 eq) was added. After 30 min, the reaction reached completion and was quenched with acetone (10 mL). The solvent was evaporated, and the product was washed with several portions of methanol. The compound was recrystallized from toluene/MeOH to give **2d** as purple crystals (76 mg, 0.0788 mmol, 77%). ^{1}H NMR: δ 9.60, 8.97 (both d, 4H, *J* 4.8 Hz, β), 7.32 (d, 4H, *J* 2.4 Hz, Ar), 6.90 (t, 2H, *J* 2.4 Hz, Ar), 4.18 (t, 8H, *J* 6.4 Hz, OCH_2), 1.92 (septet, 4H, *J* 6.4 Hz, CH), 1.79 (q, 8H, *J* 6.4 Hz, CH_2), 0.99 (d, 24H, *J* 6.4 Hz, CH_3), –2.76 (br s, 2H, NH); UV/vis: λ_{max}(ε/10^3 $M^{-1}cm^{-1}$) 426 (367), 487 (4.5), 521 (19.0), 555 (10.2), 600 (5.7), 656 (5.1) nm; MALDI-TOF MS: 964.7 (M+H requires 965.3); Anal. Calcd. C, 64.73; H, 6.27; N, 5.81; Found C, 64.92; H, 6.32; N, 5.40%.

Bromo(15'-bromo-10',20'-diphenylporphyrin-5'-yl)[1,2-bis(diphenylphosphino)ethane]palladium(II) 3a. Dibromoporphyrin **2a** (60 mg, 0.096 mmol) was added to a 50 mL Schlenk flask and heated to 100 °C under a stream of argon. Dry toluene (20 mL) was added and deoxygenated by bubbling argon for 20 min. $Pd_2(dba)_3$ (98.2 mg, 0.107 mmol) and dppe (76.9 mg, 0.193 mmol) were added and the mixture was stirred at 100 °C for 3.5 h, the reaction progress being monitored by TLC using CH_2Cl_2/hexane 1:1 as eluent. After cooling to room temperature, the solution was filtered to remove some Pd metal. The solution was reduced to about 1 mL under vacuum and cooled in a refrigerator. Excess ligand was removed by filtration and the collected solid was washed with several mL of toluene. The filtrate was reduced to about 1 mL under vacuum and ether was added to precipitate the product **3a** as purple crystals (65.9 mg, 0.059 mmol, 60.9%). ^{1}H NMR: δ 9.52, 9.41, 8.77, 8.43 (all d, 2H, *J* 4.8 Hz, β), 8.32 (m, 4H, *o*-PPh on P *trans* to Por), 8.20 (m, 2H, 10,20-Ph) 7.98 (m, 2H, 10,20-Ph), 7.71 (m, 4H, 10,20-Ph), 7.6 (m, 8H, 10,20-Ph and PPh on P *trans* to Por), 6.73 (br t, 2H, *p*-H on PPh *trans* to Br), 6.52 (dd, 4H, *o*-H on PPh *trans* to Br), 6.29 (td, 4H, *m*-H on PPh *trans* to Br), 2.52 (m, 4H, PCH_2), –2.76 (br s, 2H, NH); ^{31}P NMR δ 52.0, 37.3 (both d, $^2J_{PP}$ 26.5 Hz; UV/vis: λ_{max}(ε/10^3 $M^{-1}cm^{-1}$) 431 (327), 497 (4.1), 530 (12.8), 566 (12.4), 601 (4.7), 657 (6.5) nm; FAB MS: 1127 (M, M+H). Anal. Calcd. C, 61.91; H, 3.94; N, 4.98; Found C, 61.62; H, 4.10; N, 4.52%.

Bromo[15'-bromo-10',20'-bis(3'',5''-dimethylphenyl)porphyrin-5'-yl][1,2-bis(diphenyl-phosphino)ethane]palladium(II) 3b. Dibromoporphyrin **2a** (68.3 mg, 0.101 mmol) was treated as above in toluene (25 mL) with $Pd_2(dba)_3$ (92.5 mg, 0.101 mmol) and dppe (80.5 mg, 0.202 mmol) for 2.5 h. Isolation as for **2a** yielded the product **3b** as purple crystals (60 mg, 0.051 mmol, 50.4%). ^{1}H NMR: δ 9.52, 9.40, 8.82, 8.44 (all d, 2H, *J* 4.8 Hz, β), 8.32 (m, 4H, *o*-PPh on P *trans* to Por), 7.80 (br s, 2H, *o*-H of 10,20-Ar), 7.65 (m, 6H, PPh on P *trans* to Por), 7.62 (br s, 2H, *o*-H of 10,20-Ar), 7.37 (br s, 2H, *p*-H of 10,20-Ar), 6.75 (br t, 2H, *p*-H on PPh *trans* to Br), 6.54 (dd, 4H, *o*-H on PPh *trans* to Br), 6.30 (td, 4H, *m*-H on PPh *trans* to Br), 2.66 (s, 6H, CH_3), 2.63 (m, 2H, PCH_2), 2.56 (s, 6H, CH_3), 2.55 (m, 2H, PCH_2), –2.76 (br s, 2H, NH); ^{31}P NMR δ 51.8, 37.0 (both d, $^2J_{PP}$ 26.0 Hz; UV/vis: λ_{max}(ε/10^3 $M^{-1}cm^{-1}$) 431 (322), 498 (4.4), 530 (12.8), 568 (12.4), 601 (4.9), 658 (6.8) nm; FAB MS: 1182 (M, M+H).

Bromo(15'-bromo-10',20'-bis(3'',5''-di-t-butylphenyl)porphyrin-5'-yl][1,2-bis(diphenyl-phosphinoethane]-palladium(II) 3c. Dibromoporphyrin **2c** (70 mg, 0.081 mmol) was treated as above in toluene (20 mL) with $Pd_2(dba)_3$ (102 mg, 0.112 mmol) and dppe (64.7 mg, 0.162 mmol) for 6 h. After cooling to room temperature, the solution was filtered to remove some Pd metal. The solution was reduced to about 1 mL under vacuum and cooled in a refrigerator. Excess ligand was removed by filtration and the collected solid was washed with several mL of toluene. The filtrate was reduced to about 1 mL under vacuum and ether was added to precipitate some product and more impurities that were collected by filtration and washed with ether. The filtrate was again reduced under vacuum to about 1 mL and hexane was added to precipitate the bulk of the desired product **3c** as purple crystals (51.4 mg, 0.038 mmol, 46.9%). ^{1}H NMR: δ 9.53, 9.41, 8.82, 8.46 (all d, 2H, *J* 4.8 Hz, β), 8.33 (m, 4H, *o*-PPh on P *trans* to Por), 8.01 (br s, 2H, 10,20-Ar), 7.89 (br s, 2H, 10,20-Ar), 7.76 (br s, 2H, 10,20-Ar), 7.65 (m, 6H, PPh on P *trans* to Por), 6.75 (br t, 2H, *p*-H on PPh *trans* to Br), 6.48 (dd, 4H, *o*-H on PPh *trans* to Br), 6.25 (br t, 4H, *m*-H on PPh *trans* to Br), 2.54 (m, 4H, PCH_2), 1.60 (s, 18H, t-Bu), 1.49 (s, 18H, t-Bu), –2.72 (br s, 2H, NH); ^{31}P NMR δ 51.3, 36.7 (both d, $^2J_{PP}$ 27.5 Hz; UV/vis: λ_{max}(ε/10^3 $M^{-1}cm^{-1}$) 432 (359), 499 (4.6), 531 (13.2), 568 (14.3), 601 (5.0), 658 (7.9) nm; FAB MS 1351 (M, M+H).

Bromo{15'-bromo-10',20'-bis[3'',5''-bis(isoamyloxy)phenyl]porphyrin-5'-yl}[1,2-bis(diphenylphosphino)ethane]palladium(II) 3d. Dibromoporphyrin **2d** (135 mg, 0.14 mmol) was treated as above in toluene (10 mL) with $Pd_2(dba)_3$ (128 mg, 0.14 mmol) and dppe (111 mg, 0.28 mmol) for 3 h. Isolation as for **2a** and **2b** yielded purple crystals of **3d** (112 mg, 0.081 mmol, 58%). ^{1}H NMR: δ 9.51, 9.39, 8.89, 8.54 (all d, 2H, *J* 4.8 Hz, β), 8.33 (m, 4H, *o*-PPh on P *trans* to Por), 7.66 (m, 6H, PPh on P *trans* to Por), 7.37 (br s, 2H, *o*-H on 10,20-Ar), 7.16 (br s, 2H, *o*-H on 10,20-Ar), 6.85 (t, 2H, *p*-H on 10,20-Ar), 6.73 (br t, 2H, *p*-H on PPh *trans* to Br), 6.52 (dd, 4H, *o*-H on PPh *trans* to Br), 6.28 (br t, 4H, *m*-H on PPh *trans* to Br), 4.22 (t, 4H, *J* 6.4 Hz, OCH_2), 4.06 (t, 4H, *J* 6.4 Hz, OCH_2), 2.53 (m, 4H, PCH_2), 1.96 (m, 4H, CH), 1.84 (q, 4H, *J* 6.4 Hz, CH_2), 1.73 (q, 4H, *J* 6.4 Hz, CH_2), 1.06 (d, 12H, *J* 6.4 Hz, CH_3), 0.95 (d, 12H, *J* 6.4 Hz, CH_3), –2.79 (br s, 2H, NH); ^{31}P NMR δ 51.9, 37.0 (both d, $^2J_{PP}$ 26.5 Hz; UV/vis: λ_{max}(ε/10^3 $M^{-1}cm^{-1}$) 417sh (166), 432 (322), 502 (5.7), 529 (16.7), 566 (13.8), 600 (56.4), 656 (7.7) nm; FAB MS: 1470 (M, M+H). Anal. Calcd. C, 63.74; H, 5.74; N, 3.81; Found C, 63.72; H, 5.80; N, 4.02%.

5-Bromo-10,20-diphenylporphyrin 4a. Dibromoporphyrin **2a** (102 mg, 0.163 mmol) was added to a 100 mL two-necked round-bottomed flask and heated to 100 °C under a stream of argon. Dry toluene (40 mL) was added and deoxygenated by bubbling argon for 20 min. $Pd_2(dba)_3$ (161 mg, 0.176 mmol) and dppe (137 mg, 0.345 mmol) were added and the mixture was stirred at 100 °C for 4 h, the reaction progress being monitored by TLC using CH_2Cl_2/hexane 1:1 as eluent. After cooling to room temperature, NaOH in MeOH (0.188M, 1 eq) was added. The solution was stirred for 30 min, the solvents were removed under vacuum and the residue was digested with CH_2Cl_2. This solution was washed with aqueous ammonium chloride and dried over anhydrous Na_2SO_4. The volume was reduced to about 5 mL, mixed with silica gel (20 mL) and stood for 15 min. The pre-adsorbed silica gel was packed on the same volume of additional silica gel and eluted with CH_2Cl_2/hexane 1:1 to obtain the pink product band. The

residue from this band was recrystallized from toluene/MeOH to yield the purple product **4a** (50.3 mg, 0.093 mmol, 57%), whose NMR data agreed with those of an authentic sample.

5-Bromo-10,20-bis(3',5'-dimethylphenyl)porphyrin 4b. Dibromoporphyrin **2b** (14 mg, 0.021 mmol) was treated as above with $Pd_2(dba)_3$ (19 mg, 0.021 mmol) and dppe (16.5 mg, 0.042 mmol) in toluene (6 mL) for 2 h. After reaction with 1 eq of NaOH/MeOH and extraction as above, column chromatography eluting with CH_2Cl_2/hexane 1:1 followed by recrystallization from CH_2Cl_2/MeOH gave purple crystalline **4b** (8 mg, 0.013 mmol, 65%). Repetition of this procedure but with treatment with TFA/MeOH (1 eq) instead of NaOH and washing of the dichloromethane extract with aqueous $NaHCO_3$ yielded **4b** (71%). ^{1}H NMR: δ 10.17 (s, 1H, *meso*), 9.74, 9.28, 9.00, 8.99 (all d, 2H, *J* 4.8 Hz, β), 7.83 (br s, 4H, Ar), 7.44 (br s, 2H, Ar), 2.64 (s, 12H, CH_3), –3.00 (br s, 2H, NH); UV/vis: $\lambda_{max}(\varepsilon/10^3\ M^{-1}cm^{-1})$ 416 (413), 512 (18.5), 546 (6.4), 588 (5.6), 644 (3.0) nm; ESI-HRMS: 597.1642 (M+H requires 597.1654); Anal. Calcd. C, 72.36; H, 4.89; N, 9.38; Found C, 72.30; H, 4.93; N, 8.80%.

5-Bromo-10,20-bis(3',5'-di-t-butylphenyl)porphyrin 4c. Dibromoporphyrin **2c** (101 mg, 0.117 mmol) was treated as for **2a** with $Pd_2(dba)_3$ (107 mg, 0.117 mmol) and dppe (93.2 mg, 0.234 mmol) in toluene (180 mL) for 1.5 h. Reaction with NaOH/MeOH (1 eq) and isolation as for **4a** yielded purple crystalline **4c** (61 mg, 0.078 mmol, 67%), whose NMR data agreed with those of an authentic sample.

5-Bromo-10,20-bis[3',5'-bis(isoamyloxy)phenyl]porphyrin 4d. Dibromoporphyrin **2d** (102 mg, 0.106 mmol) was treated as for **2a** with $Pd_2(dba)_3$ (100 mg, 0.109 mmol) and dppe (84.5 mg, 0.212 mmol) in toluene (20 mL) for 19 h. Reaction with NaOH/MeOH (1 eq) and extraction as for **4a** with elution from the silica gel by $CHCl_3$/hexane 1:1 yielded purple crystalline **4d** (57 mg, 0.064 mmol, 61%) after recrystallization from toluene/MeOH. ^{1}H NMR: δ 10.16 (s, 1H, *meso*), 9.73, 9.28, 9.09, 9.08 (all d, 2H, *J* 4.8 Hz, β), 7.37 (d, 4H, *J* 2.4 Hz, Ar), 7.44 (t, 2H, *J* 2.4 Hz, Ar), 4.17 (t, 8H, *J* 6.4 Hz, OCH_2), 1.92 (septet, 4H, *J* 6.4 Hz, CH), 1.79 (q, 8H, *J* 6.4 Hz, CH_2), 0.99 (d, 24H, *J* 6.4 Hz, CH_3), –3.04 (br s, 2H, NH); UV/vis: $\lambda_{max}(\varepsilon/10^3\ M^{-1}cm^{-1})$ 418 (348), 512 (17.5), 545 (5.3), 587 (5.3), 643 (2.4) nm; ESI-HRMS: 885.3961 (M+H requires 885.3954); Anal. Calcd. C, 70.49; H, 6.94; N, 6.32; Found C, 70.08; H, 6.90; N, 6.25%.

RESULTS AND DISCUSSION

The new method depends on the fact that the oxidative addition of the dibromoporphyrin can be interrupted after only one palladium has been inserted. We noted previously that the second insertion of M(0) is much slower than the first due to the strong electron-donating properties of the $M(II)L_2Br$ moiety[3,4], and thus we could isolate 5-bromo-15-platinioporphyrins and subsequently convert these to 5-palladio-15-platinio species [2]. We usually employ the Pd(0) and Pt(0) fragments prepared in situ from $Pd_2(dba)_2$ or $Pt(dba)_2$ (dba = dibenzylideneacetone) rather than the isolated zerovalent complexes. In the anticipation that elimination of the Pd fragment might be faster with Pd(II) in the *cis* configuration, we used bidentate diphosphines, namely dppe [1,2-bis(diphenyl-phosphino)ethane] and dppf [1,1'-bis(diphenylphosphino)ferrocene].

Reactions of dibromoporphyrins with $Pd_2(dba)_2$ and dppf were not easily controlled, and mixtures of mono- and dipalladium complexes were formed rapidly. This problem is compounded by difficulties in separating excess ligand from the Pd porphyrin. However, the reactions with dppe can be stopped conveniently after the insertion of only one Pd(dppe) fragment. We have consistently found that a ratio of dibromoporphyrin:$Pd_2(dba)_2$:dppe of 1:1:2 is exactly correct for monoaddition [3,4]. By conducting the reactions in these proportions in degassed toluene under argon at 100 °C, the 5,15-dibromo-10,20-diarylporphyrins **2a**-**2d** (all prepared in quantitative yield by bromination of **1a**-**1d** with excess NBS) with Pd(0) led to the formation almost exclusively of the corresponding 5-bromo-15-palladioporphyrins **3a**-**3d** (Scheme 1). In each case, the product was isolated and purified by repeated crystallization to remove excess

ligands and non-porphyrin Pd compounds. The monopalladium porphyrins **3a**-**3d** were identified by FAB-MS and ^{1}H (1D, COSY) and ^{31}P NMR spectra.

The progress of the oxidative additions was monitored by TLC using CH_2Cl_2/hexane 1:1 as eluent. The most rapidly moving spot is the dibromoporphyrin. The reactions were considered complete when this spot disappeared. However, our experience with these compounds shows that the next most polar spot is actually the monobromoporphyrin (**4a**-**4d)** formed by depalladation of **3a**-**3d** on the silica gel, and the organopalladium complexes **3a**-**3d** are immobile in this medium. On occasions, to complete the first insertion reaction, additional small portions of Pd_2dba_2 and dppe were added to consume the dibromoporphyrins entirely. The conditions and isolated yields are summarized in Table 1.

We had already observed the desired hydrodepalladation reaction in various guises. As described above, silica gel causes loss of Pd and cannot be used efficiently for isolation or purification of the Pd complexes. Most workers observe some debromination of the starting materials as a side reaction in Pd-catalyzed couplings that use bromoporphyrin starting materials. This is presumably a thermal, protolytic or reductive decomposition of the Pd intermediate. In addition, in our studies of the cyclic voltammetry of organopalladium porphyrins we recorded irreversible reductions and proved that depalladation occurred upon reduction [4].

For chemical hydrodepalladation, we investigated three methods, namely reduction, protolysis and β-elimination. Sodium borohydride was found to depalladate **3** rapidly, but instead of **4** being the only product, remarkably this reagent also removed the second bromine atom to regenerate **1**. We have not investigated this reaction extensively, but it did not occur with the 5-bromoporphyrins alone. Acidolysis by equimolar TFA in MeOH was effective for **3a** and **3b** but not so clean for the arylporphyrins with bulky substituents. Treatment with silica gel was only partially successful in removing the Pd. The best method proved to be treatment with equimolar NaOH in MeOH. This reagent presumably works by substitution of methoxide for bromide on Pd, followed by β-elimination of formaldehyde to form a *cis* hydrido(porphyrinyl)Pd(II) complex that rapidly and quantitatively eliminates the porphyrin fragment. This chemistry recalls work reported by one of us on hydroxo-, methoxo- and hydrido(aryl) platinum(II) bis(phosphine) complexes [9].

We then developed the method into a "one-pot" procedure in which the oxidative addition product mixture is simply cooled, treated with the base reagent, extracted and passed through a short silica gel column to yield the monobromoporphyrins **4a**-**4d**, whose only minor contaminant is sometimes fully debrominated **1a**-**1d**, with no dibromo compound. The final purified yields of **4a**-**4d** obtained by this procedure are summarized in Table 1. Thus all exhaustive chromatography has been eliminated. As mentioned at the outset, this is not so vital for DPP itself, but for the highly soluble diarylporphyrins, especially the very useful **1d**, this represents a distinct advance. The savings in solvents, silica gel and researchers' time outweigh the added expense of the palladium/phosphine reagents and the extra equivalent of NBS. The palladium end products and excess ligand cling avidly to the silica gel, and possibly could be recovered in useful form for recycling, but we have not studied this yet. Hydrodehalogenation of organic halides has been achieved by a huge variety of metal-mediated processes, including catalytic Pd methods [10]. It would obviously be desirable to achieve a catalytic version of our procedure, but it seems unlikely that selectivity of *mono*hydrodebromination could be maintained. The fact that the Pd is immobilized and solvent and silica gel volumes are dramatically reduced means the environmental impact of this synthetic step is radically diminished.

In summary, we have developed a rapid and convenient methodology for monobromination of lipohilic 5,15-diarylporphyrins involving dibromination followed by one-pot palladation and hydrodepalladation. We anticipate that this method will be applicable to any diarylporphyrin as the reagents and conditions are relatively mild.

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REFERENCES

(1) See, for example (a) DiMagno SG, Lin VS-Y and Therien MJ. *J. Org. Chem.* 1993; **58**: 5983-5993. (b) Arnold DP, Bott RC, Eldridge H, Elms F, Smith G and Zojaji M. *Aust. J. Chem.* 1997; **50**: 495-503. (c) Shanmugathasan S, Johnson CK, Edwards C, Matthews EK, Dolphin D and Boyle RW. *J. Porphyrins Phthalocyanines* 2000; **4**: 228-232. (d) Lin VS-Y, DiMagno SG and Therien MJ. *Science* 1994; **264**: 1105-1111. (e) Shediac R, Gray MHB, Uyeda HT, Johnson RC, Hupp JT, Angiolillo PJ and Therien MJ. *J. Am. Chem. Soc.* 2000; **122**: 7017-7033. (f) Taylor PN, Wylie AP, Huuskonen J and Anderson HL. *Angew. Chem. Int. Ed.* 1998; **37**: 986-989. (g) Shultz DA, Gwaltney KP and Lee H. *J. Org. Chem.* 1998; **63**: 4034-4038. (h) Sugiura K-i, Fujimoto Y and Sakata Y. *Chem. Commun.* 2000; 1105-1106. (i) Nakamura K, Fujimoto T, Takara S, Sugiura K-i, Miyasaka H, Ishii T, Yamashita M and Sakata Y. *Chem. Lett.* 2003; **32**: 694-695. (j) Hyslop AG, Kellett MA, Iovine PM and Therien MJ. *J. Am. Chem. Soc.* 1998; **120**: 12676-12677. (k) Aratani N and Osuka A. *Org. Lett.* 2002; **3**: 4213-4216. (l) Odobel F, Suresh S, Blart E, Nicolas Y, Quintard J-P, Janvier P, Le Questral J-Y, Illien B, Rondeau D, Richomme P, Häupl T, Wallin S and Hammarström L. *Chem. Eur. J.* 2002; **8**: 3027-3046. (m) Shi B and Boyle RW. *J. Chem. Soc., Perkin Trans. 1* 2002; 1397-1400. (n) Hasobe T, Imahori H, Yamada H, Sato T, Ohkubo K and Fukuzumi S. *Nano Lett.* 2003; **3**: 409-412. (o) Takanami T, Hayashi M, Hino F and Suda K. *Tetrahedron Lett.* 2003; **44**: 7353-7357. (p) Gao GY, Chen Y and Zhang XP. *J. Org. Chem.* 2003; **68**: 6215-6221. (q) Gao GY, Colvin AJ, Chen Y and Zhang XP. *Org. Lett.* 2003; **5**: 3261-3264.

(2) Arnold DP, Sakata Y, Sugiura K-i and Worthington EI. *Chem. Commun.* 1998; 2331-2332.

(3) Arnold DP, Healy PC, Hodgson MJ and Williams ML. *J. Organomet. Chem.* 2000; **607**: 41-50.

(4) Hodgson MJ, Healy PC, Williams ML and Arnold DP. *J. Chem. Soc., Dalton Trans.* 2002; 4497-4504.

(5) Hartnell RD, Edwards AJ and Arnold DP. *J. Porphyrins Phthalocyanines* 2002; **6**: 695-707.

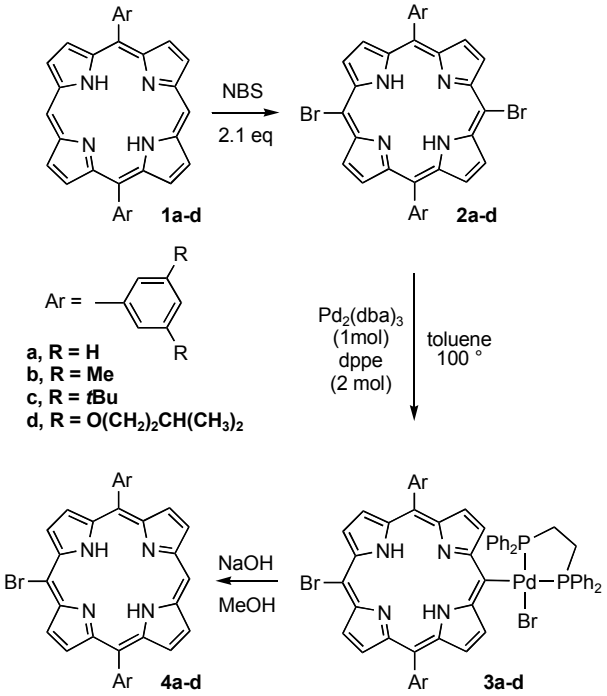
(6) Hartnell RD and Arnold DP. *Eur. J. Inorg. Chem.* 2003; in press.

(7) Hartnell RD and Arnold DP. *Organometallics* 2003; in press.

(8) Senge MO and Feng XD. *J. Chem. Soc., Perkin Trans. 1* 2000; 3615-3621.

(9) Arnold DP and Bennett MA. *Inorg. Chem.* 1984; **23**: 2110-2116.

(10) Alonso F, Beletskaya IP and Yus M. *Chem. Rev.*, 2002; **102**: 4009-4091.



Scheme 1.

Table 1. Summary of isolated yields of **3** and **4**

R in Ar	Yield of **3**[a] (%)	Yield of **4**[b] (%)
a H	61	57
b Me	50	71
c *t*-Bu	47	67
d O-*i*-Am[c]	58	61

[a] Yield of isolated and purified **3**. [b] Yield from **2** to **4** in the one-pot procedure. [c] 3-methylbutoxy.